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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,447	02/13/2004	Chandra Vargeese	MBHB02-312-G (600.041)	2130
65778	7590	09/27/2007	EXAMINER	
MCDONNELL, BOEHNEN, HULBERT AND BERGHOFF, LLP 300 SOUTH WACKER DRIVE SUITE 3100 CHICAGO, IL 60606			OLSON, ERIC	
		ART UNIT		PAPER NUMBER
		1623		
		MAIL DATE	DELIVERY MODE	
		09/27/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/780,447	VARGESE ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 September 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) The period for reply expires 3 months from the mailing date of the final rejection.
- b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because

- (a) They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) They raise the issue of new matter (see NOTE below);
- (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. Applicant's reply has overcome the following rejection(s): _____.

6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none.

Claim(s) objected to: none.

Claim(s) rejected: 5, 6, 15, 16, 20 and 21.

Claim(s) withdrawn from consideration: none.

AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.

12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____

13. Other: _____

Detained Action

This action is in response to Applicant's arguments submitted September 18, 2007 After Final.

11. Applicant's request for reconsideration submitted September 18, 2007, has been fully considered but not found persuasive to remove the finality of the previous office action in view of the reasons set forth in the final office action.

Applicant argues that there can be no finding of obviousness under the current situation because of the alleged similarity of the instant case to that of *Takeda Chemical Industries v. Alpharma*, in particular the finding that it is not obvious to vary a chemical structure in the absence of a finite number of predictable solutions, and that one of ordinary skill in the art would not have known to attach a double stranded RNA to the claimed conjugates, as opposed to attaching any other biologically active molecule. As regards the choice to attach a short dsRNA to the conjugates of Low in view of Connolly, the facts of the present case differ from those of *Takeda* in that Li explicitly exemplifies dsRNA as a biologically useful molecule to deliver intracellularly. One of ordinary skill in the art would not be thrashing about blindly trying to predict which biological molecules would be useful to attach to the conjugates, but would rather recognize that Li et al. specifically identifies small dsRNAs as being a useful to deliver intracellularly.

Additionally, Applicant argues that the claimed invention is directed to compounds involving a specific, novel type of double-stranded RNA, and that the prior art, particularly Li et al., would not have contemplated a RNA with less than 25 base pairs. However, Li et al. discloses double-stranded RNAs generally, with a **preferred embodiment** having a length of 25 or more base pairs. According to MPEP 2123, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." See *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) 27 F.3d at 554, 31 USPQ2d at 1132.). 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). Therefore contrary to Applicant's assertion, Li et al. does not teach away from shorter dsRNAs.

Furthermore, p. 16, lines 5-9 of Li et al. states that it is routine to determine the effects of synthesized oligoribonucleotide dsRNAs, and suggests that one of ordinary skill in the art would determine the minimum effective length of dsRNA needed to silence the target gene. This statement by Li et al. teaches toward modifying the length of the dsRNA with the aim of finding the minimum effective length, and further that testing oligonucleotides of various lengths is routine to one of ordinary skill in the art.

Oligonucleotides are a special case of chemical structures, and are more predictable than the organic small molecules featured in *Takeda*. The court in *Takeda* found that the prior art reference disclosed a family of compounds encompassing

hundreds of millions of compounds. In the instant case, Li et al. teaches double-stranded oligonucleotides of relatively short length. One of ordinary skill in the art would have recognized that, due to the specific biological interactions of oligonucleotides with proteins and nucleic acids *in vivo*, varying the length of an oligonucleotide is a particularly predictable variable with respect to function. In other words, adding or subtracting nucleotide base pairs from the dsRNAs of Li et al. would be expected to conserve more of the function of the molecules than any other modification. Therefore, modifying the length of the oligonucleotide would be a particularly suggested and obvious modification for one of ordinary skill in the art to make. With respect to the "hundreds of millions" of compounds taught by the prior art in *Takeda*, the family of dsRNAs of Li et al. has merely hundreds of possible lengths, at most about a thousand. Therefore there are merely a finite number of possible family members to choose from.

With regards to the comparison of the facts in *Takeda* with those in *Pfizer* vs. *Apotex*, the facts of the instant case, wherein one of ordinary skill in the art chooses from dsRNAs of various possible lengths, are closer to *Pfizer*, where there were tens of family members to choose from, than *Takeda*, where there were hundreds of millions.

For these reasons, Applicant's arguments are not found to be convincing and all rejections of record in the previous action are maintained. Applicant's request for reconsideration fails to put the application in condition for allowance.

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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9/24/07

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